

AMENDMENTS TO THE CLAIMS

Claim 1. (Currently amended) A method of promoting the healing of a skin wound comprising applying to said skin wound an effective skin wound healing amount of a composition comprising:

BP (bone protein mixture) ~~depleted of from which~~ histones and/or ribosomes have been excluded and comprising
the growth factors BMP-3 and TGF- β 2, and
a pharmaceutically acceptable carrier.

Claim 2. (Previously presented) The method of claim 1 wherein the composition further comprises at least one bone-derived growth factor selected from the group consisting of BMP-2, BMP-4, BMP-5, BMP-6, and BMP-7, wherein at least one said growth factor retains native post-translation modifications.

Claim 3. (Previously presented) The method of claim 1 wherein the composition further comprises at least one bone-derived growth factor selected from the group consisting of FGF-1, TGF- β 1, and TGF- β 3 in its native post-translation modified form.

Claim 4. (Previously presented) The method of claim 1 wherein at least one said growth factor is at least partially phosphorylated and glycosylated.

Claim 5. (Currently amended) The method of claim 1, wherein ~~said composition is free of~~ histone proteins H1c and H1x are excluded from the composition.

Claim 6. (Previously presented) A method of promoting skin wound healing comprising applying to said skin wound a composition comprising a mixture of growth factors comprising BMP-2, BMP-3, BMP-6, and TGF- β 2 in a pharmaceutically acceptable carrier.

Claim 7. (Currently amended) The method of claim 1 wherein ~~said composition is substantially free of~~ ribosomal proteins LORP, Lg, s20, L3, S3a, S4 and L32 are excluded from

the composition.

Claim 8. (Previously presented) The method of claim 1 wherein said at least one growth factor is derived from bovine bone and is at least partially phosphorylated and glycosylated.

Claims 9-17. (Cancelled)

Claim 18. (Previously presented) A method of promoting the healing of a skin wound, said method comprising applying to a skin wound a composition comprising a bone-derived mixture of proteins comprising BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, TGF- β 1, TGF- β 2, TGF- β 3 and FGF-1 in a pharmaceutically acceptable carrier.

Claim 19. (Original) The method of claim 18, wherein the pharmaceutically acceptable carrier includes a hydrogel.

Claim 20. (Previously presented) The method of claim 18, wherein said proteins are at least partially phosphorylated and glycosylated.

Claim 21. (Original) The method of claim 18, where the pharmaceutically acceptable carrier includes a dressing selected from the group consisting of hydrocolloid dressings, hydrogels, foam dressings, and alginate dressings.

Claim 22. (Previously presented) The method of claim 18, wherein said composition further comprises one or more active ingredient selected from the group consisting of arginine, glutamine, zinc, copper, vitamin C, vitamin B1, vitamin B2, vitamin B3, vitamin B6, vitamin B12, and folate.

Claim 23. (Previously presented) The method of claim 18, wherein said composition further comprises one or more growth factor selected from the group consisting of epidermal growth factor, platelet derived growth factor, insulin-like growth factor, keratinocyte growth

factor, vascular endothelial growth factor, transforming growth factor alpha, nerve growth factor, connective tissue growth factor and granulocyte-monocyte colony stimulating factor.

Claims 24.-25. (Cancelled)

Claim 26. (Previously presented) A method of improving angiogenesis in a wound area where osteogenesis is not desired comprising applying to said wound a composition comprising a bone protein mixture, wherein when said mixture is subjected to sodium dodecyl sulfate polyacrylamide gel electrophoresis, yields a reduced or non-reduced protein band pattern as identified in Figure 1, said composition including a pharmaceutically acceptable carrier.

Claim 27. (Cancelled)

Claim 28. (Currently amended) The method of claim 1 wherein said bone protein mixture is obtained from bovine bone, and, when subjected to trypsin digestion, comprises the following tryptic peptide fragments:

XLAAAGYDVEK (SEQ ID NO:1)

SLEKVCADLIR (SEQ ID NO:2)

~~(V)VCGMLGFPSEAPV~~ VCGMLGFPSEAPV (SEQ ID NO:3)

STGVLLPLQNNELPG (SEQ ID NO:4)

STGVLLPLQNNELPGAQYQY (SEQ ID NO:5)

STGVLLPLQ (SEQ ID NO:6)

~~(S)QTLQFXE~~ QTLQFXE (SEQ ID NO:7)

VYAF (SEQ ID NO:8)

~~HAGKYSREKNT(P)A(P)~~ HAGKYSREKNTA (SEQ ID NO:9)

SQTLQFDEQ (SEQ ID NO:10)

SLKPSNHA (SEQ ID NO:11)

~~A(H)I(Q)VERYV~~ AIVERYV (SEQ ID NO:12)

~~XALF(G)AQLGXALGPI~~ XALFAQLGXALGPI (SEQ ID NO:13)

SQTLQFDEQT (SEQ ID NO:14)

SQTLXF (SEQ ID NO:15)

VLATVTKPVGGDK (SEQ ID NO:16)
XVFAL (SEQ ID NO:17)
AVPQLQGYLR (SEQ ID NO:18)
ALDAAYCFR (SEQ ID NO:19)
GYNANFCAGACPYL (SEQ ID NO:20)
VNSQSLSPY (SEQ ID NO:21)
~~KAAKPSV(P)~~ KAAKPSV (SEQ ID NO:22)
SQTLQFXE (SEQ ID NO:23)
XALFGAQLGXALGPI (SEQ ID NO:24)
VVCGMLGFPSEAPV (SEQ ID NO:25)
HAGKYSREKNTAP (SEQ ID NO:26)
HAGKYSREKNTPA (SEQ ID NO:27)
HAGKYSREKNTPAP (SEQ ID NO:28)
AHIVERYV (SEQ ID NO:29)
AIQVERYV (SEQ ID NO:30)
AHIQVERYV (SEQ ID NO:31)
XALFGAQLGXALGPI (SEQ ID NO:32)
KAAKPSVP (SEQ ID NO:33).

Claim 29. (Previously presented) The method of claim 1 wherein said skin wound comprises a diabetic ulcer.

Claims 30-32. (Cancelled)

Claim 33. (Previously presented) The method of claim 1, wherein the BP is prepared by a process comprising protein extraction from demineralized bone, filtration, and chromatography.

Claim 34. (Previously presented) The method of claim 33, wherein the filtration comprises first ultrafiltration with an ultrafiltration membrane having a nominal molecular

weight cut off (MWCO) of 100 kD, to yield a retentate and a filtrate, and second ultrafiltration of the filtrate with an ultrafiltration membrane having a nominal MWCO of about 10 kD.

Claim 35. (Previously presented) The method of claim 33, wherein the chromatography comprises anion exchange chromatography, cation exchange chromatography, and HPLC in which the BP is eluted from the column with an organic solvent/water mixture gradient.

Claim 36. (Previously presented) The method of claim 1, wherein the bone protein mixture is extracted from demineralized bone.

Claim 37. (Currently amended) The method of claim 1, wherein at least one protein other than BMP-3 and TGF- β 2 has been ~~removed~~ excluded from the bone protein mixture.

Claim 38. (Previously presented) The method of claim 1, wherein when the bone protein mixture is subjected to sodium dodecyl sulfate polyacrylamide gel electrophoresis it yields a reduced or non-reduced protein band pattern as identified in any one of Figures 1-4.

Claim 39. (Previously presented) The method of claim 36, wherein the bone protein mixture is subjected to chromatography.

Claim 40. (Previously presented) The method of claim 39, wherein the bone protein mixture comprises at least one fraction eluted during chromatography.

Claims 41-64. (Cancelled)